Research Article

Plasma resistin and vaspin levels in obese people: Correlations with aging

Novi Khila Firani[1,2,3]*, Agustin Iskandar[2], Nonong Eriani[4]

ABSTRACT

Backgrounds: Resistin and visceral adipose tissue-derived serine protease inhibitor (vaspin) are adipocytokines that have a relationship with obesity. This study was designed to examine the plasma resistin and vaspin level change during aging in obese Indonesian people. **Materials and Methods:** We performed a cross-sectional study. A total of 60 healthy volunteers aged 20–69 years were enrolled and divided into five groups (20–29, 30–39, 40–49, 50–59, and 60–69 years). Body mass index and waist circumference were measured to determine obesity. Plasma resistin and vaspin levels were measured using ELISA. **Results:** Plasma resistin and vaspin levels increased with aging. Mean resistin levels (ng/mL) were 33.1 ± 9.8, 78.0 ± 8.7, 107.7 ± 11.6, and 93.2 ± 9.2 in the age groups of 20–29, 30–39, 40–49, 50–59, and 60–69 years, respectively. Mean vaspin levels (ng/mL) were 64.6 ± 3.7, 88.6 ± 3.8, 94.1 ± 4.2, 92.6 ± 4.8, and 88.1 ± 8.1 for the above age groups. Pearson correlation analysis showed that resistin and vaspin were positively associated with age. The coefficient correlation of resistin was 0.442 ($P = 0.001$), higher than vaspin ($r = 0.360$, $P = 0.002$). **Conclusions:** Plasma resistin and vaspin levels increased with aging in obese Indonesian people.

KEY WORDS: Aging, Obese, Resistin, Vaspin

INTRODUCTION

The prevalence of obesity among adults and the elderly has increased over the recent decade and has led to an enhanced concern about the metabolic disease.[1] In Indonesia, the national prevalence of obesity in populations <15 years was 10.3% in 2011, and the prevalence in women was higher than men.[2]

Obesity is a serious health problem because it is correlated with various diseases such as 31 mellitus, atherosclerosis, and cancer.[3] Pathophysiological mechanisms of obesity involve many factors including nutrition, environment, genetics, and aging. Aging is one of the primary risk factors for the development of obesity and is thought to be an imbalance of increased energy consumption over reduced energy expenditure. Brown adipocytes are responsible for thermogenesis and could counter obesity by increasing energy expenditure. However, aging is accompanied by a relative loss of classical brown adipocytes.[4,5]

Adipose tissue is an active endocrine organ. It can produce and secrete adipokines such as resistin and vaspin. Resistin is a cysteine-rich adipokine induced during adipogenesis. It is an adipocyte-derived cytokine that may contribute to the development of obesity,[6-9] insulin resistance,[10-12] and metabolic syndrome.[13] Recent studies have shown a causative association between resistin and systemic inflammation.[14,15] Resistin mRNA is also increasing in visceral fat obesity mice.[16] Vaspin (visceral adipose tissue-derived serpin) is an adipokine that potentially has protective action against obesity-associated metabolic disturbance. Higher vaspin serum level and increased vaspin mRNA expression in human adipose tissue were found to be associated with obesity.[17] It has been assumed that vaspin serves as an insulin sensitizer with anti-inflammatory effects and might act as a compensatory mechanism in response to decreased insulin sensitivity. The induction of vaspin

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mRNA expression could represent a compensatory mechanism associated with obesity, severe insulin resistance, and type 2 diabetes mellitus.[18,19] The previous study reported that vaspin level is associated with aging in normal people.[20] Furthermore, Yang *et al.* revealed that in diabetic obese elderly patients, serum vaspin concentration was significantly higher than in normal weight patients.[21] However, the association of vaspin and resistin level with aging in obese individuals is still limited, and report on the Indonesian population is not yet elucidated until now. This study was designed to examine the plasma resistin and vaspin level changes during aging in obese Indonesian people.

MATERIALS AND METHODS

Anthropometric and Clinical Assessments

The study protocol was performed according to the Helsinki Declaration and approved by the Health Research Ethics Committee of Medical Faculty of Universitas Brawijaya. Informed written consent was obtained from the patients. All study participants underwent a standard clinical examination. The anthropometric and clinical assessments were took at a privately owned clinic in Kelurahan Kedungkandang, Jalan Muharto, Kota Malang. Height and body mass were recorded using a stadiometer attached to a scale. Weight was obtained with participants wearing light clothing and no shoes. Waist circumference measurements were made using a cloth tape measure at the level of the umbilicus. Body mass index (BMI) was calculated as weight divided by the square of height (kg/m^2). BMI for obesity was >25 kg/m^2 as described by the WHO Western Pacific Region,[22] waist measures >90 cm (male) and > 80 cm (female). Pregnant and breastfeeding women were excluded, as well as subjects using hormonal contraception to reduce the hormonal effects that could interfere with measurement results. Subjects were enrolled if aged 20 years old and over because it started from 20 years old, health level will start to gradually decrease as stated by the WHO (WHO report on aging and health).[23] Then, subjects were divided into five groups based on age: Group I (20–29 years), n = 3; Group II (30–39 years), n = 13; Group III (40–49 years), n = 19; Group IV (50–59 years), n = 17; and Group V (60–69 years), n = 8.

ELISA Assays and Biochemical Investigations

Whole blood samples (5 mL) were obtained from all of the obese subjects in tubes containing EDTA for resistin and vaspin investigations. Blood samples were centrifuged at 1000 g for 10 min. Plasma specimens were then frozen and stored at −80°C until analysis. Human plasma resistin (RayBiotech Inc.) and vaspin (RayBiotech Inc.) levels were measured with ELISA, using a Bio-Rad® Microplate Reader Model 550.

Statistical Analysis

Comparisons between groups were made using ANOVA and a *post hoc* Tukey test. Multiple linear regression stepwise test was used to determine the correlation between BMI with body weight, height, and waist circumference. Pearson correlation test was used to determine the correlation between age and plasma resistin and vaspin levels. All analyses were done with SPSS 13.0 for Windows (SPSS Inc., Chicago, Illinois, USA).

RESULTS

Subject Characteristics

A total of 60 healthy obese individuals were enrolled in the study. The subjects were obese individuals with widely ranging ages. In total, 91% of subjects were female and 9% male. The anthropometric characteristics of subjects are shown in Table 1.

In Pearson correlation analysis, both height and body weight are negatively associated with age $r = -0.219$, $P = 0.101$ and $r = -0.061$, $P = 0.653$, respectively. Waist circumference positively correlate with age ($r = 0.213$, $P = 0.103$) and BMI also positively correlate with age ($r = 0.095$, $P = 0.472$). In multiple linear regression stepwise analysis, waist circumference is removed, weight positively associated with BMI, while height is negatively associated with regression model $y = 67.356 + 0.420\ X_1 - 0.438\ X_2$ ($R^2 = 98.4\%$) [Figure 1].

The Plasma Resistin and Vaspin Level of Obese Subjects

There were significant differences in plasma resistin levels between Group I, Group III, IV, and V [Figure 2], but there were no significant differences

Table 1: Anthropometric characteristics of obese subjects

Anthropometric Parameters	Group I 20–29 y.o (n=3)	Group II 30–39 y.o (n=13)	Group III 40–49 y.o (n=19)	Group IV 50–59 y.o (n=17)	Group V 60–69 y.o (n=8)	P value
Height (cm)	159.33±4.33	154.38±1.61	153.52±1.38	154.29±1.81	149.75±1.42	0.225
Weight (kg)	81.66±8.00	78.92±1.79	74.84±2.05	77.82±2.09	76.81±3.85	0.497
BMI (kg/m^2)	32.03±1.5	33.06±0.82	31.59±0.68	32.64±0.72	33.75±1.92	0.453
Waist circumference (cm)	102±4.5	99.46±1.36	98.55±2.00	103.47±1.56	104.44±1.98	0.064

Anthropometric characteristics of obese subjects in five groups based on age showing no significant differences in height, weight, BMI, and waist circumference between the groups. Data are reported as mean (±SD) with P<0.05. SD: Standard deviation, BMI: Body mass index

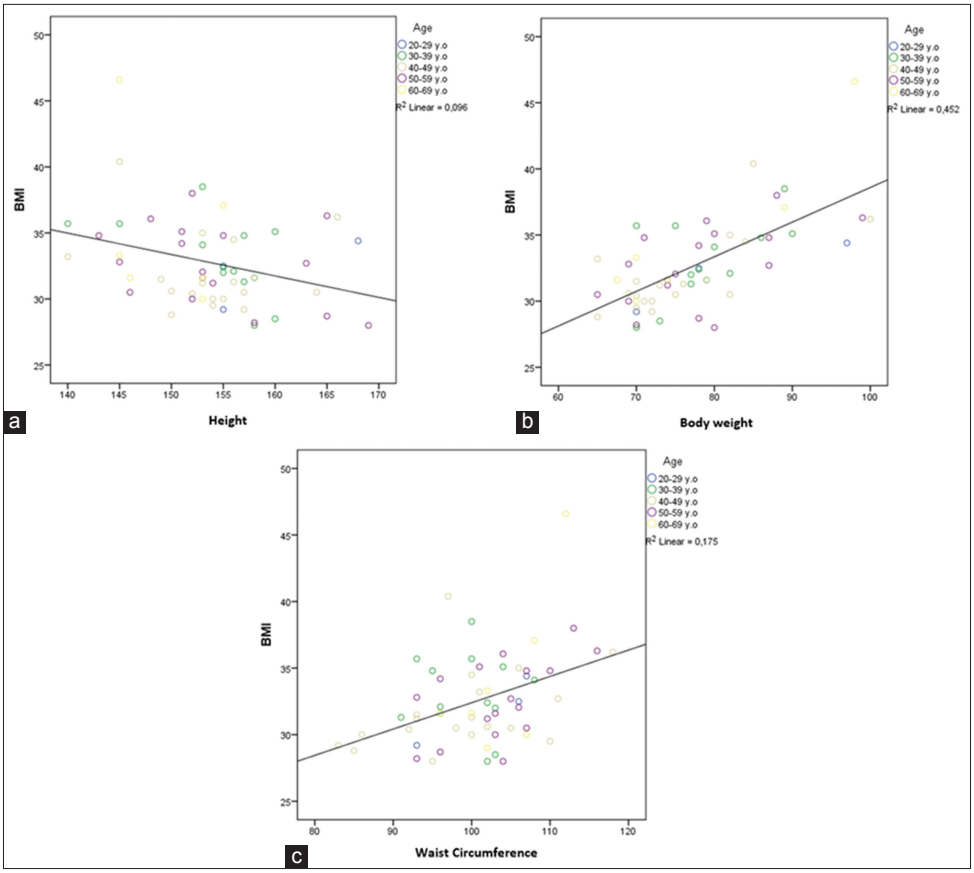

Figure 1: Scatter diagrams showing the interaction of (a) body mass index (BMI) with body height ($R^2 = 0.096$), (b) BMI with body weight ($R^2 = 0.452$), and (c) BMI with waist circumference based on the age group ($R^2 = 0.175$). All data have positive correlation, and the BMI has the strongest correlation with body weight as shown in Figure 2b

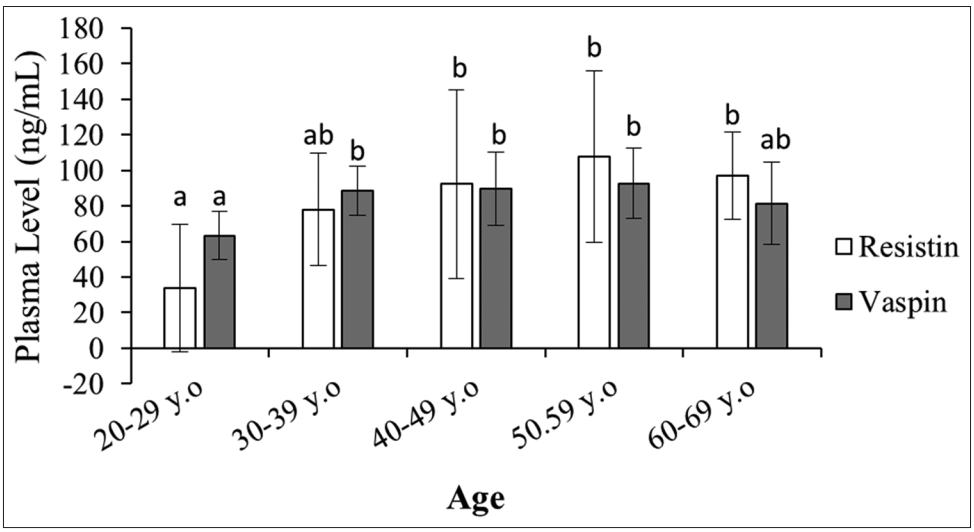

Figure 2: The level of plasma resistin and vaspin of obese subjects in five groups based on age showing no significant differences between the groups. Data are reported as mean (±standard deviation) with $P < 0.05$

in resistin level between Group I and Group II, and between Group II and Group III, IV, and V [Figure 1]. In terms of plasma vaspin levels, there were significant differences in vaspin levels between Group I, Group II, III, and IV [Figure 2], and there were no significant differences in vaspin levels between Group V and Group II, III, and IV [Figure 2]. In Pearson correlation analysis, resistin plasma levels positively associated with age ($r = 0.442$, $P = 0.001$) and vaspin plasma levels also positively associated with age ($r = 0.360$, $P = 0.002$). The plasma resistin and vaspin level of obese subjects are shown in Figure 2 [Table 2].

Table 2: The level of plasma resistin and vaspin in obese subjects

Resistin and Vaspin Levels	Group I 20–29 y.o (*n*=3)	Group II 30–39 y.o (*n*=13)	Group III 40–49 y.o (*n*=21)	Group IV 50–59 y.o (*n*=17)	Group V 60–69 y.o (*n*=9)	*P* value
Resistin (ng/mL)	103.12±21.36	77.99±31.61	92.23±52.91	107.68±48.07	96.99±9.2	0.864
Vaspin (ng/mL)	75.53±20.79	88.60±13.89	89.79±20.7	92.64±19.82	81.33±23.29	0.784

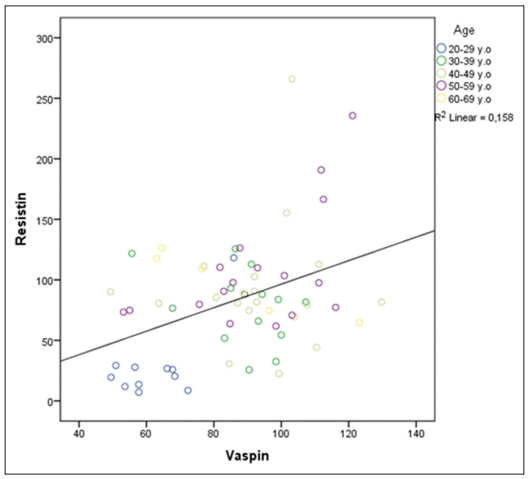

Figure 3: A scatter diagram showing the positive interaction between vaspin and resistin by age group. From this figure, the interaction between the two considered low with $R^2 = 0.158$

In Pearson correlation analysis, resistin plasma levels positively associated with age ($r = 0.467$, $P = 0.000$) and vaspin plasma levels also positively associated with age ($r = 0.325$, $P = 0.009$) [Figure 3].

DISCUSSION

We have studied predominantly female mixed-age population of 60 obese individuals from Indonesia. This gender bias is compatible with the U.S data and the national prevalence of obesity in Indonesia, which both found that the prevalence of obesity is higher among women than among men.[2,3] Based on the anthropometric characteristic of obese subjects, the highest mean of BMI and waist circumference was in the 60–69 years group. This finding relates to the U.S. data, which stated that the prevalence of obesity was higher among middle-aged adults aged 40–59 (40.2%) and older adults aged 60 and over (37.0%).[2] BMI and waist circumference are increased with age, suggesting that central obesity increased with age.

The risk of obesity is increased with aging. Aging in humans is associated with alterations in body fat distribution.[24] Aging is associated with changes in body composition. After 20–30 years of age, fat-free mass progressively decreases, whereas fat mass increases. Fat-free mass decreases by up to 40% from 20 to 70 years of age.[25] Aging is also associated with a redistribution of body fat. With aging, there is a greater relative increase in intra-abdominal fat than in subcutaneous or total body fat.[26] However, these observations, which were obtained from cross-sectional studies, can be affected by survival bias because obese persons have higher mortality rates at younger ages.

In our study, plasma resistin and vaspin concentration increased with aging until the age of 50–59 years and declined the 60–69 years age group. Since plasma resistin levels significantly correlated with age, it is conceivable that with aging, which is typically associated with alterations in body fat distribution (increased proportion of visceral fat), resistin expression would be increased, but the mechanism is still unclear.

Higher vaspin serum level and increased vaspin mRNA expression in human adipose tissue were found to be associated with obesity.[17] These findings can be explained that in advanced old age, fat depot size declines while lipids are redistributed to muscle, bone marrow, and other tissues. Decreased fat depot size is related to reduced fat cell size and function and impaired differentiation of preadipocytes into fat cells, causing dysfunctional adipocytes. During aging, the function, proliferation, size, and number of adipose cells become altered.[27] Since plasma vaspin significantly correlated with age, it is conceivable that with aging, which is typically associated with alterations in body fat distribution, vaspin expression would be upregulated. Hence, it could be understood from these findings that in obese individuals, the level of plasma resistin and vaspin will increase with aging and decline at 60–69 years, but the mechanism is still unclear and needs further research.

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